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EXAMINER	
LU, FRANK WEI MIN	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,551	FRESKGARD ET AL.	
	Examiner	Art Unit	
	FRANK LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-18 and 56-62* is/are pending in the application.

5a) Of the above claim(s) *5,9 and 10* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-4,6-8,11-18 and 56-62* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *16 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/27/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of species (1) (complementary single stranded identifier oligonucleotides are obtained prior to the step of partitioning the bifunctional complexes, see claim 4), species (4) (the identifier oligonucleotide linked to the display molecule consisting of a duplex identifier oligonucleotide comprising complementary single stranded identifier oligonucleotides, see claims 6-12), species (5) (the display molecule of a bifunctional complex provided in step i) is linked to a single stranded identifier oligonucleotide, see claims 7-12), and species (7) (said single stranded identifier oligonucleotides of the different bifunctional complexes are complemented prior to partitioning of the bifunctional complexes, see claim 8) in the reply filed on October 7, 2011 is acknowledged. The traversal is on the ground(s) that: (1) "[A]pplicants respectfully traverse the election requirement on the basis that the technical features embraced by groups (1)-(3) do not lack unity of invention. PCT Rule 13.1 states that international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. It is respectfully submitted that the species listed above are, in fact, linked so as to form a single general inventive concept. The species are linked because they are simply permutations of the method for identifying a display molecule embraced by claim 1. The general method of claim 1 forms the basis for linking the above species, and thus, there is unity of invention here"; (2) "[A]pplicants respectfully traverse the election requirement on the same basis set forth above for Species Election 1. Again, it is respectfully submitted that the species are linked because they are simply permutations of the method for identifying a display molecule embraced by claim 1. The general method of claim 1

forms the basis for linking the above species, and thus, there is unity of invention here"; and (3) "[A]pplicants respectfully traverse the election requirement on the same basis set forth above for Species Elections 1 and 2. Again, it is respectfully submitted that the species are linked because they are simply permutations of the method for identifying a display molecule embraced by claim 1.The general method of claim 1 forms the basis for linking the above species, and thus, there is unity of invention here".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such that species (1) to (9) will be examined together. First, the office action mailed on April 7, 2011 (see page 7) clearly stated that "[S]hould applicant traverse on the ground that the inventions have unity of invention (37 CFR 1.475(a)), applicant must provide reasons in support thereof. Applicant may submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. Where such evidence or admission is provided by applicant, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention". Although applicant argues that "[T]he species are linked because they are simply permutations of the method for identifying a display molecule embraced by claim 1", applicant has not provided or submitted evidence or identified such evidence to show why species (1) cannot be an obvious variant of species (2), species (3) cannot be an obvious variant of species (4), species (5) cannot be an obvious variant of species (6), and species (7) cannot be an obvious variant of species (8) or (9). Second, since the office action mailed on April 7, 2011 (see page 7) clearly stated that "[U]pon the allowance of a generic

claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise require all the limitations of an allowed generic claim", the examiner has agreed to consider other species if claim 1 is allowable. Therefore, the requirement is still deemed proper and is made FINAL. Claims 1-4, 6-8, 11-18, and 56-62 will be examined.

Specification

2. The disclosure is objected to because of the following informalities: (1) there are Figures 1A, 1B and 1C. However, Brief Description of the Figures of the specification only describes Figure 1; (2) applicant is required to update the information for DK PA 2003 00430 in page 20, and PCT/DK03/00739 in page 21 of the specification; and (3) there are multiple nucleotide sequences having more than 10 nucleotides in pages 94, 96, 97, 105, and 123-141. However, there are no SEQ ID Nos. for these nucleotide sequences in pages 94, 96, 97, 105, and 123-141.

Appropriate correction is required.

Claim Objections

3. Claim 1 is objected to because of the following informalities: (1) the word "further" in line 2 of the preamble should be deleted; and (2) "the single stranded identifier oligonucleotides obtained in step i)" in step ii) should be "the complementary single stranded identifier oligonucleotides obtained in step i)".

4. Claim 2 or 3 or 4 is objected to because of the following informality: "complementary single stranded identifier oligonucleotides" should be "the complementary single stranded identifier oligonucleotides".

5. Claim 6 is objected to because of the following informality: "the enriched fraction" in step v) should be "the enriched fraction of bifunctional complexes".

6. Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim because claim 6 has included "complementing said single stranded identifier oligonucleotides of the different bifunctional complexes, thereby obtaining a duplex identifier oligonucleotide comprising complementary identifier oligonucleotides". Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

7. Claims 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim because claim 7 has generated a duplex identifier oligonucleotide comprising complementary oligonucleotide strands. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

8. Claim 14 or 15 is objected to because of the following informality: "the hetero-duplexes" should be the hetero-duplex identifier oligonucleotides.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Enablement

Claims 1-4, 6-8, 11-18, and 56-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance to perform the methods recited in claims 1-4, 6-8, 11-18, and 56-62. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the methods recited in claims 1-4, 6-8, 11-18, and 56-62 can be performed.

Although the claims are directed to a method for identifying a display molecule of a bifunctional complex comprising an identifier oligonucleotide linked to the display molecule, since in view of steps i), ii), v) and vi) of claim 1, it is unclear whether complementary single stranded identifier oligonucleotides from an enriched and partitioned fraction of bifunctional complexes having an affinity for a target molecule can hybridize with an identifier oligonucleotide linked to the display molecule, what hybridizes with the complementary single

stranded identifier oligonucleotides obtained in step i) so that a composition comprising homo-duplex identifier oligonucleotides, hetero-duplex identifier oligonucleotides can be formed, and how decoding the identifier oligonucleotides of the homo-duplexes can be used to identify the one or more display molecules identifier, it is unpredictable how the methods recited in claims 1-4, 6-8, 11-18, and 56-62 can be performed.

Therefore, in view of above discussion, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether the methods recited in claims 1-4, 6-8, 11-18, and 56-62 can be performed.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-4, 6-8, 11-18, and 56-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 1 is rejected as vague and indefinite in view of step (ii) because it is unclear hybridizing the single stranded identifier oligonucleotides obtained in step i) to what so that a composition comprising homo-duplex identifier oligonucleotides and hetero-duplex identifier oligonucleotides can be formed. Please clarify.

14. Claim 1 is rejected as vague and indefinite in view of step (iii) because it is unclear that homo-duplexes mean homo-duplex identifier oligonucleotides in step ii) or not and hetero-duplexes mean homo-duplex identifier oligonucleotides in step ii) or not. Please clarify.

15. Claim 1 is rejected as vague and indefinite because step vi) does not make sense. Does step vi) mean identifying the one or more display molecules based on the step v)? Please clarify.

16. Claim 3 is rejected as vague and indefinite in view of the phrase "hybridising a probe oligonucleotide with the identifier oligonucleotide of the bifunctional complex". If the identifier oligonucleotide of the bifunctional complex in the phrase means the duplex identifier oligonucleotide, the claim does not make sense. Please clarify.

17. Claim 3 is rejected as vague and indefinite. Since the first part of the claim requires to obtain the duplex identifier oligonucleotide comprising the complementary single stranded identifier oligonucleotides while the second part of the claim requires to obtain a complementary identifier oligonucleotide hybridised with the identifier oligonucleotide linked to the display of the bifunctional complex, the first part and the second part of claim do not correspond each other. Please clarify.

18. Claim 4 recites the limitation "the step of partitioning the bifunctional complexes" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no step of partitioning the bifunctional complexes in claims 1-3. Please clarify.

19. Claim 6 is rejected as vague and indefinite in view of step vi). Since steps i) to v) do not contain bifunctional complexes in which the display molecule is linked to a single stranded identifier oligonucleotide, it is unclear why single stranded identifier oligonucleotides of different bifunctional complexes in which the display molecule is linked to a) a single stranded identifier oligonucleotide can be complemented as recited in step vi). Furthermore, it is unclear that a duplex identifier oligonucleotide comprising complementary identifier

oligonucleotides in step vi) is identical to a duplex identifier oligonucleotide comprising said complementary single stranded identifier oligonucleotides in claim 1 or not. Please clarify.

20. Claim 6 is rejected as vague and indefinite in view of the phrase "with the proviso that no single stranded complementation occurs for bifunctional complexes comprising b) duplex identifier oligonucleotides comprising complementary identifier oligonucleotides" because it is unclear that no single stranded complementation occurs between what. Please clarify.

21. Claim 6 is rejected as vague and indefinite. Since step i) of claim 1 has an enriched and partitioned fraction of bifunctional complexes having an affinity for a target molecule and comprising a duplex identifier oligonucleotide comprising said complementary single stranded identifier oligonucleotides while step vi) of claim 6 produces a duplex identifier oligonucleotide comprising complementary identifier oligonucleotides, it is unclear what is the relationship among these preliminary step in claim 6 and step i) of claim 1. Please clarify.

22. Claim 7 is rejected as vague and indefinite because it is unclear that a bifunctional complex is from step i) of claim 1 or from one of the bifunctional complex of step i) of claim 6. Furthermore, it is unclear that said single stranded identifier oligonucleotides of the different bifunctional complexes complements to what. Please clarify.

23. Claim 8 is rejected as vague and indefinite because it is unclear that the bifunctional complexes in the claim mean the enriched fraction of bifunctional complexes comprising one or more display molecules having an affinity for said target molecule or mean bifunctional complexes not having an affinity for said target molecule or mean both the enriched fraction of bifunctional complexes comprising one or more display molecules having an affinity for said

target molecule and bifunctional complexes not having an affinity for said target molecule. Please clarify.

24. Claim 13 recites the limitation "the display molecule of at least some of the bifunctional complexes" in the claim. There is insufficient antecedent basis for this limitation in the claim because claim 1 does not indicate that a display molecule is on at least some of the bifunctional complexes and only indicates that an identifier oligonucleotide is linked to the display molecule. Please clarify.

25. Claim 56 recites the limitation "the recovered homo-duplexes" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase "recovered homo-duplexes" in claim 1. Please clarify.

26. Claim 56 recites the limitation "the step of decoding the identity of the display molecule" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no step of decoding the identity of the display molecule in claim 1. Please clarify.

27. Claim 57 recites the limitation in "the partitioned fraction of identifier oligonucleotides". There is insufficient antecedent basis for this limitation in the claim because there is no phrase "partitioned fraction of identifier oligonucleotides" in claim 1. Please clarify.

28. Claim 59 is rejected as vague and indefinite because it is unclear that the complementary identifier oligonucleotide strands of homo-duplexes and hetero-duplexes in the fraction comprising predominantly homo-duplexes are separated and allowed to hybridise with what. Please clarify.

29. Claim 60 is rejected as vague and indefinite because it is unclear that the complementary identifier oligonucleotide strands of homo-duplexes and hetero-duplexes in the fraction comprising predominantly homo-duplexes are re-hybridised with what. Please clarify.

30. Claim 61 is rejected as vague and indefinite because it is unclear that the identifier oligonucleotides are re-hybridised with what. Please clarify.

Conclusion

31. Since the claims in this instant applicant are so ambiguous (see above rejection under 35 U.S.C 112, second paragraph), applicant is required to amend the claims in response to this office action so that a better prior art search can be done.

32. No claim is allowed.

33. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached on (571)272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /
Primary Examiner, Art Unit 1634
October 24, 2011